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Fast Track Cardiac Anaesthesia

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INTRODUCTION

Cardiac anaesthesia, like most major medical disciplines, has undergone many transformations over the years. Up until the 1960's cardiac surgery was only performed in the patient in whom all other medical options had failed. In the late 60's and through to the 1970's this picture changed dramatically with the discovery of high dose opioid anaesthesia and the cardiostability it provided.^{1,2} The high dose opioids necessitated postoperative ventilation which in turn allowed time to stabilise the patient's haemodynamics, temperature, and arterial blood gas variables. It also facilitated re-operation in the immediate postoperative period e.g. for bleeding.

The use of Coronary Artery Bypass Graft (CABG) surgery in the elderly population in the United States has doubled every 5 years since 1985 and by 2003 it was estimated that 500 000 cardiac procedures were performed annually in the US at a cost of around \$9 billion.³ Thus, mainly due to financial constraints, the focus of cardiac anaesthesia started shifting in the early 1990's to lower dose opioids, earlier extubation and decreased ICU stay. This came to be labelled as 'Fast Track Cardiac Anaesthesia'.⁴ (FTCA)

There are no fixed, accepted definitions in this field but general consensus accepts the following:

- FTCA (sometimes referred to as Early Extubation Anaesthesia {EEA}) is extubation within 8 hours of the end of surgery. Many major centres, however, aim for extubation 1 – 4 hours postoperatively.⁵
- There is also the notion of Ultra Fast Track Anaesthesia (UFTA) which refers to extubation of patients in theatre post cardiac surgery. It is mostly reserved for patients undergoing off-pump cardiac surgery⁶ but some work has been done on patients after cardiopulmonary bypass (CPB)⁷ and it is generally not a universally accepted method.⁸

For the purposes of this review I have not considered off-pump cardiac surgery or UFTA.

In this review I will cover:

1. Patient selection for FTCA
2. Safety and efficacy of FTCA – compared to conventional cardiac anaesthesia – including complications
3. Methods of FTCA
4. Pain Management of the FTCA patient – should we be using epidurals?
5. Cost benefits associated with FTCA

1. PATIENT SELECTION

Constantinides et al⁹ did a study in 2006 with one of the aims being the identifying of risk factors for unsuccessful fast tracking. They tested more than 30 risk factors associated with FTCA and the failure thereof and identified 8 independent risk predictors for fast track failure:

- Impaired LV function (ejection fraction <30%)
- Acute coronary syndrome within 30 days of surgery
- Re-do operations
- Extracardiac arteriopathy
- Preoperative need for intra-aortic balloon pump
- Raised serum creatinine (>150µmol/l)
- Urgent operation
- Complex surgery (i.e. CABG + other heart / vascular procedure)

Most of these risk factors would seem logical to us as being poor predictors of post operative recovery, therefore almost all of the studies done on FTCA – most pre 2006 – have shown a similarity to these predictors in the exclusion of patients from their study. The exception to this is a very recent study published earlier this year Svircevic et al in which they included all elective patients with no other exclusions.¹⁰

All studies I came across have included only adult patients undergoing elective cardiac surgery. Most included only 1st time CABG patients¹¹⁻²² although some included CABG and / or valve surgery.^{3,22} There does not seem to be any benefit in excluding patients undergoing valve surgery from fast track protocols from what I have read. I would, however, not recommend fast tracking patients undergoing complex cardiac surgery i.e. CABG plus other cardiac surgery or double valve surgery.

It therefore seems reasonable to me that patients eligible for a fast track protocol should include:

- Adult patients
- Elective surgery
- Either CABG / valve surgery
- 1st time surgery
- Good LV function
- No recent myocardial infarction (MI) i.e. within 30 days of surgery
- No systemic disease that would contraindicate the fast tracking of the patient e.g. renal failure; chronic obstructive pulmonary disease

2. SAFETY AND EFFICACY

Despite a multitude of trials in the 1990's and early 2000's showing the apparent safety of early extubation post cardiac surgery as well as its tendency to decrease ICU length of stay (LOS) and cost per patient, there were still many lingering concerns regarding the use of FTCA.

In 2003 Myles et al³ did a meta-analysis with their objective being to prove that FTCA was as safe as Conventional Cardiac Anaesthesia (CCA). They included all trials involving elective CABG or valve surgeries done with CPB.

They excluded any off-pump cardiac surgery and any patients who received any form of neuraxial blockade.

Overall they included 10 trials with a total of 1800 patients.

FTCA was defined for their analysis as low dose opioid ($\leq 20\mu\text{g}/\text{kg}$ fentanyl or equivalent) and extubation within 10 hours of the end of the procedure. CCA was defined as $>20\mu\text{g}/\text{kg}$ fentanyl (or equivalent) and extubation >10 hours after the end of the procedure.

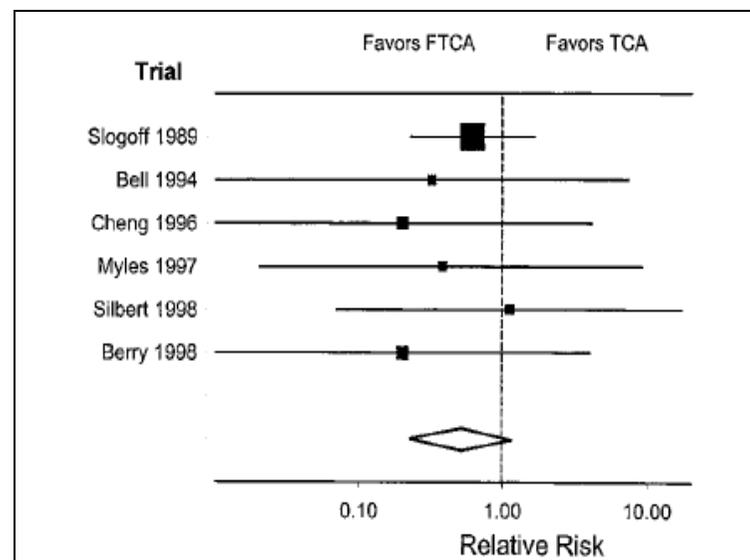
The primary outcome was 30 day all-cause mortality.

Secondary outcomes were:

- Myocardial infarction
- Major sepsis
- Stroke
- Acute renal failure requiring dialysis
- Prolonged ICU stay (>5 days)
- Major bleeding requiring surgical exploration
- Time to tracheal extubation
- ICU and hospital LOS
-

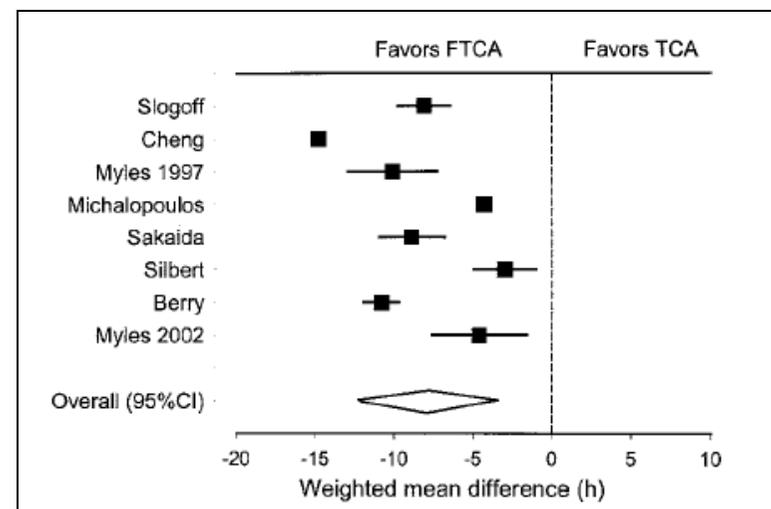
They showed:

- No statistically significant difference in mortality rate



Forest Plot comparing the relative risk of Mortality between FTCA and CCA

- No statistically significant difference with respect to major morbidity
- Markedly decreased time to tracheal extubation with a pooled weighted mean reduction of 8.1 hours



Forest Plot Comparing the Weighted Mean Difference in Extubation Times of FTCA vs CCA

- Decreased ICU LOS
- No significant decrease in hospital LOS

They concluded that there was no evidence of increased morbidity or mortality with FTCA techniques and combined with the known cost benefits there was no reason to continue with high dose opioid techniques. They did concede, however, that even as a meta-analysis their study was underpowered and therefore unable to accurately predict rare events including mortality.

Their findings are consistent with a Cochrane Review also from 2003²³ showing no difference between early and conventional extubation with regards to mortality in ICU or at 30 days. There was no significant difference in postoperative myocardial ischaemia, re-intubation before or after 24 hours. Early extubation also showed a decreased ICU and hospital length of stay.

A meta-regression by van Mastrigt et al²⁴ in 2006 showed that neither anaesthetic dose, temperature management, nor extubation protocols were significant predictors for MI and death following cardiac surgery.

Earlier this year Svircevic and colleagues from the Netherlands published their study in Anesthesia & Analgesia.² Their aim was to compare FTCA and CCA using a large number of patients (7989) surpassing the 2 previous largest studies with 1012²¹ and 404²⁵ patients respectively. They also hoped to be able to draw more telling conclusions than those reached by Myles et al.³

Methods:

- From Jan 2000 – May 2003 patients receiving CCA were monitored (4020 patients in total)
- They then phased in a FTCA protocol and monitored all patients between Aug 2003 and Dec 2006 (3969 patients)

Anaesthesia techniques:

- CCA

Pre-med	Midazolam 15mg po
Induction	Sufentanil 2 - 4µg/kg
	Midazolam 0.05 – 0.1mg/kg
	Pancuronium 0.1mg/kg
Maintenance	Sufentanil 0.5 - 2µg/kg/hr
	Midazolam 0.1mg/kg/hr
ICU sedation	Midazolam 2 – 4mg/hr

- FTCA

Pre-med	Midazolam 7.5mg po
Induction	Remifentanil 1 - 2µg/kg
	Propofol 1 -2mg/kg
	Pancuronium 0.1mg.kg
	+/- Midazolam up to 5mg
Maintenance	Remifentanil 5 - 10µg/kg/hr
	Propofol 1 – 4mg/kg/hr <u>or</u>
	Sevoflurane 0.5 – 1.5%
End of surg	Morphine 0.1 – 0.2mg/kg
ICU sedation	Propofol 1 – 2mg/kg/hr

Sedation continued in the ICU until:

- Patients were haemodynamically stable (no or minimal inotropes and urine output >0.5ml/kg/hr)
- Temperature >35⁰C
- O₂ saturation ≥ 93%
- FiO₂ ≤ 0.4

Surgical Technique:

Of note patients were cooled to between 28 – 34⁰C despite many experts feeling that normothermic CPB is essential to FTCA.

Outcomes:

Primary	Mortality
Secondary	MI Stroke Renal failure Duration of mechanical ventilation ICU LOS Hospital LOS

Results:

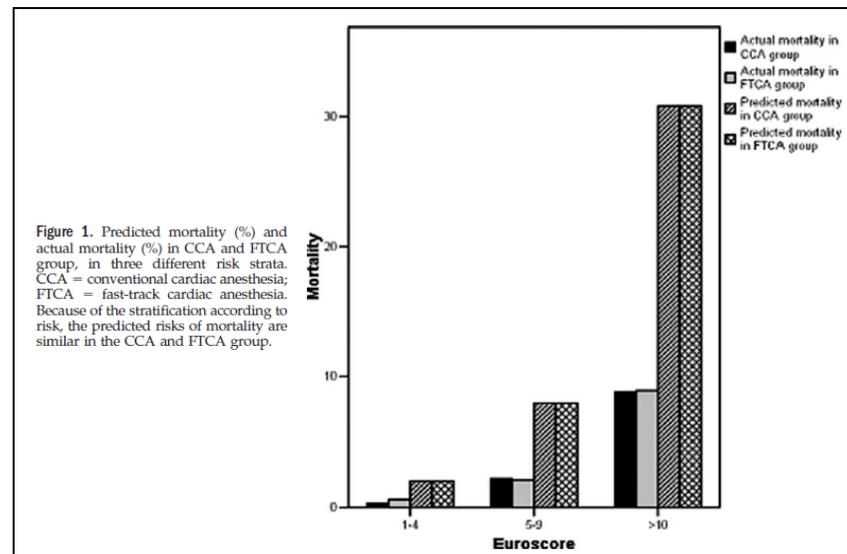
- Both crude and adjusted mortality rates showed no significant difference between the 2 groups as shown in the table below

Table 2. Crude and Adjusted Odds Ratio for Mortality, FTCA Versus CCA Group

	Odds ratio	95% CI
Crude	1.20	0.88–1.64
Adjusted for: age and female gender (1)	1.14	0.83–1.56
1 + diabetes mellitus (2)	1.13	0.82–1.54
2 + hypertension (3)	1.14	0.83–1.56
3 + LVEF (4)	1.11	0.80–1.54
4 + betablokkers (5)	1.05	0.76–1.46
5 + duration of CPB (6)	0.90	0.64–1.26
All confounders ^a	0.92	0.65–1.32

An odds ratio of >1.00 indicates an increased risk of mortality in the FTCA group.
 CCA = conventional cardiac anesthesia; FTCA = fast-track cardiac anesthesia; CPB = cardiopulmonary bypass; CI = confidence interval.

- The authors then stratified the patients into 3 risk groups according to their EuroSCORE²⁶ (a risk stratification system) viz. 1 – 4; 5 – 9; >10
- Across all 3 strata the predicted mortality was higher than the actual mortality in both groups
- There was, however, no difference between the 2 groups in actual mortality illustrated in Figure 1



- Table 3 below shows how the frequency of MI / stroke / renal dysfunction was not significantly different between the 2 groups

Table 3. The Frequency and Odds Ratios of Myocardial Infarction, Stroke, and Renal Failure Between the CCA and FTCA Groups

	CCA group n=4020	FTCA group n=3969	Crude odds ratio	95% CI	Adjusted odds ratio ^a	95% CI
Myocardial infarction	5.2%	5.5%	1.07	0.84–1.35	0.92	0.71–1.18
Stroke	0.9%	1.3%	1.52	0.98–2.35	1.38	0.86–2.20
Renal failure	0.8%	0.8%	0.95	0.59–1.54	0.64	0.37–1.12

An odds ratio of >1.00 indicates an increased risk in the FTCA group.
 CCA = conventional cardiac anesthesia; FTCA = fast-track cardiac anesthesia; CI = confidence interval.

- There was a significant decrease in the duration of mechanical ventilation in the FTCA group (geometric mean of 6.7 hours versus 12.2 hours)
- They did however find an increase in the duration of both ICU and hospital stay in the FTCA group – they put forward possible explanations as FTCA group being extubated in the evening when transfer to the ward was then made difficult as well as the fact that there were more significant co-morbidities in the FTCA group necessitating longer hospital stay

The authors thus concluded that their results were in keeping with other studies and meta-analyses showing no effect of FTCA on mortality and morbidity.

Other important complications that have been studied in FTCA include:

1. ICU Readmission

Kogan et al²⁷ in 2003 did a study of 1613 patients undergoing FTCA. They found an ICU readmission rate of 3.29% (53/1613).

25 patients were re-admitted in the 1st 24 hours post discharge; 15 from 24 – 48 hours; and 13 after 48 hours.

The most common cause was pulmonary (43.4%) although only 15.1% of these required re-intubation.

Kogan et al identified the following 4 risk factors as increasing the risk for ICU re-admission:

- Age >70 years
- Female sex
- Surgery other than 1st isolated CABG
- 2000 Bernstein-Parsonnet risk estimate >20²⁸ (a bedside risk estimation score determined by the 2 authors. It accounts for age, disease and surgical factors)

Ender et al²⁹ in 2008 showed lower ICU readmission in their FTCA group compared to control (not statistically significant) and Cheng et al¹⁹ have shown no increase in ICU readmission compared to CCA.

2. FTCA Failure

This refers to patients who would be fast tracked through a cardiac recovery area (CRA) but required transfer to the ICU. The rate of failure ranged from 1%³⁷ to 6.3%¹⁶

3. Re-intubation

In a 2003 review Myles et al³ reported that re-intubation was rare with a rate of usually <2% in patients undergoing FTCA.

4. Myocardial Ischaemia

Considered separately to Myocardial Infarction Cheng et al²⁰ showed no increase in ischaemia in FTCA. They also showed in the same study no increase in plasma catecholamine levels / change in haemodynamic variables / increase in vasoactive medication requirements.

5. Cognitive Function

Cheng et al²⁰ showed better performance on mental status exam in patients having undergone FTCA (not statistically significant). A 2006 meta-regression by van Mastrigt et al²⁷ described no major difference in cognitive function between FTCA and CCA.

3. METHODS OF FAST TRACK CARDIAC ANAESTHESIA

There are as many fast track protocols as there are units providing a fast track service for cardiac surgery. Patient selection is essential (as discussed earlier). Pre-medication of patients is varied with benzodiazepines especially lorazepam proving to be the most popular. The major focus of many studies has been particularly aimed at the opioid to use and in what dose, as well as the role of propofol in maintenance of anaesthesia.

Fentanyl does still appear to be the gold standard opioid – most considering 10 - 15µg/kg as low dose but this does stretch out to 20µg/kg for some authors.

Induction

The most common induction agent is propofol (in combination with an opioid), usually at a dose of 0.5mg/kg + 10mg boluses until loss of consciousness^{13-15,19,20,30} although some use propofol in higher doses^{3,11,29,31,32} or even start directly with an infusion¹⁷. Both etomidate and thiopentone are described as being used – commonly in doses roughly half that of the usual induction dose. There are some centres that omit the induction agent entirely.^{18,27} There appears to be no benefit in choosing a shorter acting muscle relaxant.

Choice of Opioid

Fentanyl at a dose of 10 - 15µg/kg at induction is still commonly used in many centres^{11,17,19,20,27,30,31} and it is this dose that has traditionally been used in studies comparing remifentanil and sufentanil with the gold standard.

Howie et al¹³ in 2001 looked at remifentanil infusion versus fentanyl boluses. They found that the remifentanil group had less response to the stimulation of incision and sternal spreading compared to the fentanyl group. There was also a need for more anaesthetic intervention in the fentanyl group as evidenced by an increased need for opioid boluses, isoflurane pre-CPB, vasodilators, and propofol infusion on CPB (38 +/- 30mg/kg/hr vs 5.8 +/- 25mg/kg/hr). There was, however, increased hypotension pre-CPB in the remifentanil group.

Postoperatively there was no significant difference in haemodynamics, ECG changes, catecholamine levels, cardiac enzymes or time to extubation.

They concluded that remifentanil was equally safe and effective as fentanyl with no difference in time to extubation.

Cheng et al¹⁴ in 2001 had similar results in comparing fentanyl and remifentanyl showing no difference in morbidity and mortality, no difference in times to extubation or discharge and no difference in mental state by day 3.

Molhoff et al¹⁵, also in 2001, report different results. They found an increased intubation response in the remifentanyl group but thereafter significantly decreased response to skin incision and sternotomy. There was higher incidence of inadequate anaesthesia (defined by haemodynamic changes, somatic responses, and autonomic responses) in the fentanyl group (52% vs 11%) as well as higher propofol maintenance requirements. There was significantly increased extubation times in the fentanyl group although time to ICU discharge was shorter. The remifentanyl group needed more analgesia postoperatively, however mean pain scores were similar. Despite increased hypertension and shivering in the remifentanyl group there were no increased adverse events viz. ischaemia / MI / CCF / death.

Engoren et al³² went one step further, also in 2001, comparing fentanyl, remifentanyl and sufentanyl. They showed no difference in time to extubation / ICU or hospital LOS. Sufentanyl had lower morphine requirements compared to the other 2 groups but Visual Analogue Scores (VAS) for pain was similar in all. The highest opioid cost was in the remifentanyl group but overall costs were similar.

Lison et al in 2007³³ compared remifentanyl versus sufentanyl. They were able to show less response to skin incision and sternal spread with remifentanyl but not to intubation, sternotomy or sternal wire placement. There was a 1.3 hour decrease in time to extubation in the remifentanyl group. There was no significant difference in adverse events and pain scores were significantly higher in the remifentanyl group.

No study has shown a convincing, clear benefit of one opioid agent over another. As long as one ensures that they remain within the 'low dose' range of their chosen opioid, any agent is effective provided one is aware of the shortcomings of the said drug e.g. postoperative analgesia is a far greater concern in remifentanyl compared to the others. Choose the drug you are most comfortable with and learn how to use it most effectively in your own hands. That seems to be the most important message to take away from this section.

Maintenance

Prior to a study by Myles et al³⁰ in 1997, propofol was a much avoided drug in cardiac anaesthesia. He compared its use in maintenance to enflurane and showed no increased mortality or awareness. There were similar haemodynamic changes with no difference in inotrope requirements. He also showed a significantly decreased time to extubation with no increase in the incidence of ischaemia or postoperative MI. Since then propofol has been used commonly in cardiac anaesthesia – either as part of a total intravenous anaesthetic technique^{3,15,17} or as sedation on CPB continuing into the ICU following on from volatile use pre-CPB.^{3,11-14,19,20,29,31} Choice of volatile is also a personal one with isoflurane, sevoflurane and desflurane all described in the literature.

Post CPB

The most common agent used for sedation of these patients post bypass and into the ICU is propofol.^{3,12-15,19,20,31,42} Some units add midazolam either as boluses or an infusion.³ Pain management of the patient post op will be discussed separately.

Dexmedetomidine has shown some promise as a safe drug for the cardiac patient in the intensive care unit³⁴. It conveys good sedation with minimal haemodynamic changes³⁵. I could find no study using dexmedetomidine as part of a fast track anaesthetic protocol.

Extubation Criteria

Most centres have fixed extubation and discharge criteria that they are using for their FTCA protocols. There is very little variation in the criteria that I came across in the various studies. Below, as an example, is the criteria used by Cheng et al in their studies out of Toronto.

Tracheal Extubation Criteria

- Patient responsive and cooperative
- Negative inspiratory force $\geq 20\text{cmH}_2\text{O}$
- Vital capacity $>10\text{ml/kg}$
- $\text{PaO}_2 >80\text{mmHg}$ on $\text{fiO}_2 \leq 0.5$
- Cardiac index $>2.0\text{l/min/m}^2$
- Temperature $>36.5^\circ\text{C}$
- pH >7.30
- Chest tube drainage $<100\text{ml/hr}$ for 2 hours
- Absence of uncontrolled dysrhythmia

ICU Discharge Criteria

- Patient alert and cooperative
- No inotropes or arrhythmias
- Adequate ventilation viz. PaO₂ >80mmHg; PaCO₂ <60mmHg; SpO₂ >90% on 50% face mask O₂
- Chest tube drainage <50ml/hr for 2 hours
- Urine output >0.5ml/kg/hr
- No active seizure

Hospital Discharge Criteria

- Haemodynamically stable
- Stable cardiac rhythm
- Afebrile and non-infected incisions
- Patient able to void and had bowel movement
- Patient is independent in ambulating and feeding

Surgical Factors

There is an undercurrent of opinion that normothermic ($\geq 32^{\circ}\text{C}$) cardiopulmonary bypass is essential to a fast track technique. However, this does not seem to be supported in the literature. Some centres adhere to relative normothermia^{20,31,36,37} while others are prepared to cool patients as low as 28°C while still successfully fast tracking them.^{10,18,25,27,30,30,38,39} The important variable seems to be rewarming⁴⁰. All studies mentioning rewarming will warm the patient to $36.5 - 38^{\circ}\text{C}$ before taking the patient off bypass. It is also essential to continue to actively warm the patient through the recovery period as secondary cooling can delay time to extubation.⁸ Never rewarm too quickly as this can lead to overshoot of the desired temperature and overheating.

I found no literature suggesting that bypass time plays a significant role in the fast tracking of cardiac surgical patients.

A table comparing generic anaesthetic practice at IALCH with 2 FTCA models described in the literature**

	Svircevic et al²	Cheng et al²²	IALCH
Pre-med	Midazolam 7.5mg po	Lorazepam 1-3mg po	Lorazepam 1-2mg po
Induction	Remifentanyl 1-3µg/kg Propofol 1-2mg/kg Pancuronium 0.1mg/kg	Fentanyl 10-15µg/kg Propofol 0.5mg/kg Pancuronium 0.15mg/kg	Fentanyl 3.5-7µg/kg Propofol 0.6-1.4mg/kg Pancuronium 8mg + Rocuronium 50mg
	+/- Midazolam $\leq 5\text{mg}$	Midazolam 1-3mg	
Maintenance	Remifentanyl 5-10µg/kg/hr Propofol 1-4mg/kg/hr or Sevoflurane 0.5-1.5%	Isoflurane 0.5-2%	Fentanyl 100µg/hr Isoflurane 0.6-1% Midazolam 1mg/hr or boluses (1-3mg)
On CPB		Propofol 2-6mg/kg/hr	Fentanyl 100µg/hr +/- Midazolam 1mg/hr
Post CPB	Propofol 1-2mg/kg/hr Midazolam 2-4mg/hr Morphine 0.1-0.2mg/kg	Propofol titrated to effect Indomethacin 50-100mg pr Morphine 1-4mg/hr	Fentanyl 100µg/hr Midazolam 1mg/hr +/-Pancuronium

**It is noted that not all anaesthetics run as above but this is a summary of the most common practices during my Cardiac Rotation at the end of 2008 / beginning of 2009.

As can be seen in the table above the technique used quite often in our centre is a comparable 'low dose' regimen compatible with early extubation. Higher doses of fentanyl at induction instead of a continuing infusion, coupled with a move to propofol sedation on CPB and continued through to the ICU could see many of our patients extubated by the early evening. These patients could be monitored overnight facilitating early transfer of the patient to high care or even the surgical ward the next morning. This could potentially alleviate many of the problems associated with limited bed space in the Cardiac ICU.

4. PAIN MANAGEMENT OF THE FTCA PATIENT

Pain management poses a significant problem after cardiac surgery and has been one of the criticisms levelled at FTCA. There are many painful interventions e.g. sternotomy, pericardiotomy, drain insertion, and leg vein harvesting. Inadequate analgesia increases morbidity through adverse effects on haemodynamics, metabolism, immunology and haemostasis.⁶ There is also the need for effective cough and deep breathing as a means to prevent atelectasis and decrease pneumonia. By hindering these, pain can be detrimental to weaning post op.⁴⁰

Chaney, in a 2006 review, states that patient satisfaction is determined as much by the comparison between anticipated and experienced pain as it is by the actual level of pain experienced.⁴¹ Thus patients, who generally expect severe pain post cardiac surgery may not complain of significant pain postoperatively despite moderate intensity pain being experienced. I have often heard quoted, 'A sternotomy is not that painful once the bone is apposed – patients almost never complain.' How valid is this observation?

Intravenous opioids have been the mainstay for many years, however with the advent of early extubation anaesthesia other techniques, in particular neuraxial, have been studied.

Many options for analgesia are available to us post cardiac surgery⁴¹:

- Local anaesthetic infiltration
- Nerve blocks
- Opioids
- NSAIDS
- Alpha-adrenergic drugs
- Intrathecal and Epidural techniques

Local anaesthetic infiltration

Used either as a once off injection or via indwelling catheters e.g. On-Q[®]PainBuster[®] at the median sternotomy incision site. This has shown some promise but questions of safety especially local tissue necrosis have remained.

Nerve blocks

Intercostal, intrapleural, or paravertebral. These blocks are fairly simple but have questionable efficacy and are best used in conjunction with other modalities.

IV Opioids

These remain the gold standard of postoperative analgesia despite concerns regarding pruritis, nausea, vomiting, urinary retention, and respiratory depression.

Postoperative morphine was far and away the most common analgesic drug used in most studies I came across, although no study was testing its use – its benefits seemed accepted. Methods included infusions, boluses and patient controlled analgesia. Reis et al¹¹ made a clinical observation of adequate analgesia postoperatively using PCA morphine.

There is no reason found to suggest that postoperative pain presents a contraindication to FTCA – morphine is a suitable alternative to the previous high dose fentanyl regimes.

NSAIDS

The notion of NSAIDS being unsafe drugs in the postoperative period remains in all spheres of surgery and there is seemingly much resistance to its use post cardiac surgery. This debate will continue to rage.

There are, however, centres using them as an integral part of their postoperative analgesic regimen. Davy Cheng and colleagues from the University of Toronto – who are highly published in this field – use 50-100mg indomethacin pr at the end of surgery¹⁹⁻²⁰ Ketorolac IV is also described for analgesia in the ICU.^{13,32}

Alpha-adrenergic agents

These may be used to enhance postoperative analgesia, however questions remain regarding their effect on haemodynamics. They also increase sedation in the ICU.

Intrathecal and Epidural techniques

These methods do produce reliable postoperative analgesia after cardiac surgery.⁶ They also present the potential additional benefit of stress response attenuation and thoracic cardiac sympathectomy. Local anaesthetics are more effective than opioids in stress response attenuation and may improve outcome.

Cardiac sympathetic nerve activation induces coronary artery vasoconstriction and paradoxical coronary vasoconstriction in response to intrinsic vasodilators. These processes may play a central role in postoperative myocardial infarction by disruption of the myocardial oxygen supply-demand balance. Local anaesthetics, but not opioids, administered

via thoracic epidural catheters could block these sympathetic nerves. Thoracic epidurals using local anaesthetics are said to increase the diameter of stenotic epicardial coronary artery segments without causing dilatation of coronary arterioles, decrease determinants of myocardial oxygen demand, improve LV function, and decrease anginal symptoms.⁴¹ The cardiac sympathectomy is also believed to beneficially affect collateral blood flow during ischaemia and decrease post-stenotic coronary vasoconstriction.⁴¹

Intrathecal techniques

Most reports have used morphine although some have looked at sufentanil, fentanyl, or even local anaesthetics. An anonymous survey by the Society of Cardiovascular Anesthesiologists showed almost 8% of practicing anaesthesiologists incorporate an intrathecal technique into their management of adult cardiac surgical patients.⁴¹

Patients receiving intrathecal morphine have been consistently shown to require less IV morphine post op for analgesia.^{12,18,41} This is offset, however, by conflicting reports regarding time to extubation. Chaney et al in 1997 showed a significantly prolonged time to extubation in patients who had intrathecal morphine.¹⁸ A study by Bowler et al showed intrathecal morphine with remifentanyl had shorter time to extubation than a fentanyl group¹² with others finding no significant difference.⁴¹⁻⁴² There has also been no benefit shown with regards to adverse events in the ICU in patients receiving intrathecal morphine.^{18,41,42}

A meta-analysis by Liu et al⁴³ enrolled 668 patients with intrathecal analgesia. Besides slightly decreased pain scores there were no other benefits to be gained. They did find increased pruritus in the intrathecal group.

Investigators have since looked to claim that varying the dose of the morphine may alter the results however the overwhelming message is that intrathecal morphine offers no additional clinical benefits besides superior postoperative analgesia.

There has been some work with intrathecal clonidine which in one study when combined with morphine was shown to produce better analgesia and shorter time to extubation compared to each of the drugs used alone.⁴¹

Epidural techniques

A survey by the Society of Cardiovascular Anesthesiologists found that 7% of practicing anaesthesiologists use an epidural technique in their

management of adult cardiac patients⁴¹. They do provide superior analgesia but whether the attenuation of the stress response or the cardiac sympathectomy offers any benefit to outcome remains to be proven.

In 2001 Scott et al³⁸ compared epidural bupivacaine + clonidine to their narcotic based protocol. Epidurals were run for 96 hours while the control group received 24 hours alfentanil infusion followed by PCA morphine. There was earlier extubation achieved in the epidural group as well as less postoperative supraventricular arrhythmias, respiratory tract infections, renal failure and confusion, however there were discrepancies in the number of smokers between the 2 groups and the extent of beta blocker therapy clouds the arrhythmia statistics. They did not assess specifically for pain.

Royse et al³⁶ compared epidural ropivacaine + fentanyl to narcotic anaesthesia in a 2003 study. Despite lower pain scores in the epidural group on day 1 and 2 they could show no other substantial differences between the 2 groups. Other studies have shown similar results.

In the meta-analysis by Liu et al⁴³ 1178 patients were enrolled in the epidural group. They found decreased risk of dysrhythmias, pulmonary complications, and a shorter extubation time with epidural techniques as well as lesser pain scores. There was no difference in mortality or myocardial infarction.

Like intrathecal techniques, there appear to be no significant, additional clinical benefits obtained from epidural techniques other than better and more reliable analgesia⁴¹.

Side effects of Intrathecal / Epidural local anaesthetics

The most important and common side effect is hypotension – especially when introduced intrathecally. There have been reports of myocardial depression secondary to bupivacaine thoracic epidural and case reports claiming the epidural to either initiate, or mask the symptoms of, myocardial ischaemia.

Side effects of intrathecal / epidural opioids

The big 4 in this list are always pruritus, nausea / vomiting, urinary retention and respiratory depression. Pruritus is said to be the most common although incidence varies widely. Nausea and vomiting is said to occur 30% of the time⁴¹ and the most important side effect: respiratory depression, is quoted as having the same incidence as conventional doses of IV / IM opioids⁴¹.

Risk of haematoma formation

It is important to note that almost half the cases of epidural haematoma have occurred after catheter removal – not just at insertion. Risk is increased when insertion of an epidural catheter is performed in a coagulopathic patient or when it is technically difficult or traumatic.⁴¹

Precautions that can be followed include:

- delay surgery for 24 hours in the event of a traumatic tap,
- delay heparinisation for at least 60 minutes post insertion,
- maintain tight perioperative control of anticoagulation.⁴¹

Many of the studies claiming the safety of epidural insertion pre-heparinisation are done prior to vascular surgery where the anticoagulation requirements are markedly less than pre-CPB.

An analysis done by Ho et al in 2000,⁴⁴ used available data to estimate the maximum and minimum risk of haematoma formation in patients undergoing neuraxial block for cardiac surgery. Note that these are estimates as there are very few reports in the literature of clinically significant haematomas post cardiac surgery– despite at least one author being aware of unreported cases involving permanent neurological damage.⁴¹ The minimum risk is equivalent to the risk of haematoma reported in the general population while the maximum risk is the highest possible incidence they could calculate. Analysing 10 840 patients who had received intrathecal injections before heparinisation for CPB they were able to report a haematoma risk of between 1:220 000 and 1:3600. Using the 4583 patients who had received an epidural they estimated risk to be between 1:150 000 and 1:1500 – possibly even as high as 1:1000.

Some centres are inserting epidurals into patients the day before surgery in order to circumvent the issue of heparinisation fairly soon after insertion. This practice however, creates an extra workload which may be difficult to cope with in a personnel poor environment such as ours. It also leads to increased discomfort for the patient as well as an increased window for complications, notably infection.

There does not seem to be a strong argument for the use of neuraxial techniques in cardiac anaesthesia. They do show a tendency to decrease extubation times – which would benefit FTCA – and decrease pain scores postoperatively. Narcotic analgesia, however, is proven to be adequate for early extubation anaesthesia and therefore neuraxial techniques are not essential to FTCA. The risks associated with neuraxial techniques, in

particular haematoma formation, seem to heavily outweigh any benefit that may be achieved.

The gold standard – intravenous opioids – would therefore remain the best option for analgesia in patients undergoing FTCA. Morphine is known to all of us. It is reliable and in the correct dose will provide adequate analgesia with minimal clinically significant side effects.

5. COST BENEFITS OF FTCA

As mentioned in the introduction, cardiac surgery is becoming a greater burden on the health care systems of countries as time passes. It was economics that drove the initial interest in fast tracking patients after cardiac surgery and it has now been proven that FTCA is a cost effective practice.⁵ Factors to consider when assessing financial benefit to cardiac surgery are outlined below:

Predictors of higher cost in cardiac surgery

- Longer ICU stay
- Longer hospital stay
- Theatre time
- Patient age
- Postoperative complications – especially sternal infection, respiratory failure, left ventricular failure and finally death – are perhaps the most significant

Factors influencing the cost of cardiac surgery²¹

- *Patient factors*
 - Age, sex, LV function, type of surgery and urgency of surgery are independent predictors of increased ICU LOS
 - Use of intra-aortic balloon pump, CCF, MI, renal failure, and obesity (BMI \geq 30 are predictors of increased hospital LOS
 - Postoperative complications carry treatment costs as well as increasing hospital LOS
- *Anaesthetic factors*
 - Duration of ventilation is related to ICU stay
 - Early extubation is facilitated by:
 - Opioid and sedation drug choices
 - Procoagulant drugs e.g. tranexamic acid or aprotinin
 - Anti-arrhythmics
- *Technological factors*
 - High-tech, high-cost equipment e.g. pulmonary artery catheters used when not necessarily indicated

- *Surgical factors*
 - Experience of the surgeon
 - CPB techniques
 - Hypothermia vs normothermia
- *ICU factors*
 - Intensivist led ICU's decrease mortality
 - Closed ICUs do less investigations
 - A cardiac recovery area allows use of less ICU beds

As early as 1980 Quasha et al⁴⁵ started claiming cost benefits to techniques of fast track cardiac anaesthesia – they estimated a saving of \$70.00 per patient (worth a lot more then compared to today, I'm sure!). Most of these claims were using surrogates for cost – usually sparing of ICU beds^{37,39} but also decreased need for investigations.⁴⁶

In 1996 Cheng et al¹⁹ designed a prospective, randomised, controlled trial to evaluate total cost savings of early extubation anaesthesia. Two groups were randomised viz. an 'early' (1 – 6 hours) and a 'late' (18 – 22 hours) extubation group. There were 50 patients per group. 41 patients in each group had no complications.

Costs were ascertained for the actual patient course as well as for when the patient met defined ICU and hospital discharge criteria (as outlined earlier). This showed the potential benefits if, for example, patients were moved from ICU to the ward when they were fit to, and not when it was convenient for staff i.e. the next morning or after everyone has had their tea-break (probably never to be achieved).

They analysed:

- Direct variable costs: i.e. those related to patient care and varying with duration or number of patients e.g. physician fees and supporting services such as physiotherapy, radiology, laboratories
- Direct fixed costs: i.e. related to patient care but relatively fixed regardless of duration or number of patients e.g. clerical staff, housekeeping
- Overhead costs: including wards, theatre, nutrition etc.

Results:

- There was no difference in the preoperative and intraoperative costs between the groups.
- Total cost savings of 9% per CABG (\$17 640 vs \$19 339) in uncomplicated surgeries (Table 9) were achieved although this benefit could increase to 13% if discharge criteria were adhered to (Table 10).

Table 9. Departmental Costs Savings in Uncomplicated CABG Surgery: Actual

Services	Early (\$) (n = 41)	Late (\$) (n = 41)	Savings (\$)	% Service	% Total Savings	P Value
Physicians	4,122 ± 360	4,235 ± 457	113	2.7	6.7	0.219
OR	3,711 ± 90	3,699 ± 96	-12	-0.3	-0.7	0.561
ICU	3,483 ± 1,221*	4,496 ± 1,860	1,013	22.5*	59.6*	0.005
Ward	4,070 ± 721*	4,595 ± 1,513	525	11.4*	30.9*	0.043
Laboratory	824 ± 194	906 ± 247	82	9.1	4.8	0.099
Radiology	607 ± 51	592 ± 36	-15	-2.5	-0.9	0.128
RT	174 ± 49*	197 ± 46	23	11.7*	1.4*	0.031
Pharmacy	568 ± 214	544 ± 142	-24	-4.4	-1.4	0.552
Physiotherapy	81 ± 55	75 ± 67	-6	-8.0	-0.4	0.659
Total	17,640 ± 1,677*	19,339 ± 2,886	1,699	8.8*	100	0.001

CABG = coronary artery bypass graft; OR = operating room; ICU = intensive care unit; RT = respiratory therapy.

* Significantly different between groups.

Table 10. Departmental Costs Savings in Uncomplicated CABG Surgery: Criteria

Services	Early (\$) (n = 41)	Late (\$) (n = 41)	Savings (\$)	% Service	% Total Savings	P Value
Physicians	4,022 ± 340	4,179 ± 460	157	3.8	6.6	0.083
OR	3,711 ± 90	3,699 ± 96	-12	-0.3	-0.5	0.561
ICU	1,687 ± 1,214*	3,471 ± 1,167	1,784	51.4*	75.1*	<0.001
Ward	3,769 ± 744*	4,128 ± 916	359	8.7*	15.1*	0.050
Laboratory	824 ± 194	906 ± 247	82	9.1	3.5	0.098
Radiology	607 ± 51	592 ± 36	-15	-2.5	-0.6	0.128
RT	121 ± 47*	171 ± 46	50	29.2*	2.1*	<0.001
Pharmacy	568 ± 214	544 ± 142	-24	-4.4	-1.0	0.552
Physiotherapy	81 ± 55	75 ± 67	-6	-8.0	-0.3	0.659
Total	15,390 ± 1,742*	17,765 ± 1,837	2,375	13.4*	100	<0.001

CABG = coronary artery bypass graft; OR = operating room; ICU = intensive care unit; RT = respiratory therapy.

* Significantly different between groups.

The costs per complicated CABG are shown below in Table 11. As can be seen they are quite substantial in some cases.

Table 11. Cost Analysis of Complicated CABG Surgery

Complications	Early (n = 9) (18%)	Late (n = 9) (18%)	Cost (\$)
Postoperative MI (PMI)	0	3 (6%)	57,267 ± 28,282
PMI and death	0	1 (2%)	80,703
Sepsis	0	1 (2%)	76,163
Reexploration for bleeding	1 (2%)	2 (4%)	25,323 ± 1,979
Atrial arrhythmia	5 (10%)	4 (8%)	25,031 ± 3,848
Reintubation for pneumonia	1 (2%)	0	45,030
Renal insufficiency and leg wound infection	2 (4%)	0	32,166 ± 4,030
CVA and death	0	2 (4%)	62,681 ± 43,760

MI = myocardial infarction; CABG = coronary artery bypass graft; CVA = cardiovascular accident.

- When the total cost analysis is done – including all complications – the authors showed a 53% decrease in cardiovascular ICU cost and a 25% decrease in total CABG cost

Table 2. Total CABG Costs Adjusted for All Complications

	Early (n = 50)	Late (n = 50)	P Value
Preoperative (\$)	1,347 ± 104	1,353 ± 92	0.76
Operating room (\$)	7,619 ± 499	7,755 ± 653	0.24
CVICU (\$)	6,463 ± 4,943*	12,046 ± 16,573	0.026
Postoperative ward (\$)	4,169 ± 1,426	4,963 ± 3,068	0.25
Total CABG cost (\$)	19,596 ± 5,766*	26,116 ± 18,175	0.019

Furthermore, the Toronto Hospital Cardiac Centre showed that in a year of FTCA they performed 24 more cardiac cases despite having 10 less operating days enforced on them by provincial government. Their ICU readmission rate did not increase and their cancellation rate secondary to patient backlog decreased from 2% to 0.3%.

Not content to limit their findings to the acute setting Cheng et al did a follow up study published in 2003¹⁹ in which they analysed the resource use of patients studied in their 2 previous trials^{19,20} over a 1 year period. 120 patients in all (60 per group) were enrolled.

Patients were analysed for:

- Mortality
- Morbidity i.e. readmission rates for primary cardiac diagnoses and use of major procedures e.g. angiograms
- Resource use such as other readmissions and rehabilitation facility use

Results were divided into 3 time periods viz. 0 – 3 months; 3 – 12 months; and 0 – 12 months:

- Four patients died in hospital – 3 in conventional group and 1 in FTCA. Of the 116 patients discharged none died during the 12 month follow up period
- In the first 3 months 5 patients from the FTCA group were admitted to acute care hospitals vs. 8 in the conventional group. This had, however, increased to 15 apiece by 12 months

- There was an increased frequency of outpatient specialist visits in the FTCA group but no difference in GP visits
- Claims to the Ontario Health Insurance Plan and drug use was similar between the 2 groups
- By estimating acute care hospital and rehab facility costs the authors calculated significant decreased costs in the FTCA group over 12 months following their surgery – up to almost 50% by the end of 12 months (Table 7).

Table 7. Cost Analysis During the 3- and 12-Month Follow-up Periods after the Index CABG Surgery

FTCA (n = 60)	Conventional (n = 60)	P (Bootstrap)	Difference of Means (Conventional and FTCA) (Bootstrap 95% CI)	FTCA cost (% Reduction)
0–3 Months, \$760.36 (1,021.4)	2,376 (4,754.2)	0.0002	(608.8, 3462.2)	68%
3–12 Months, \$1,245.2 (1,282.7)	1,595.5 (2,950.3)	0.17	(–346.0, 1540.9)	22%
0–12 Months, \$2,005.5 (1,746.5)	3,971.5 (7,095.9)	0.004	(498.7, 4909.5)	49.5%

Data expressed as mean (SD in parentheses).

CONCLUSION

Cardiac surgery, both in our and other institutions across the globe, is continually requiring scrutiny and refinement. The burden of cardiovascular disease continues to grow. Coupled with this is the extra burden on the surgical department as more of these patients surviving long enough to qualify for surgery due to better medical management. FTCA provides a means of improving the care that our patients receive. FTCA has been shown to be safe and as effective as CCA provided patient selection criteria are adhered to. Complications are not increased by early extubation post cardiopulmonary bypass. Pain can be adequately managed through tried and tested techniques, such as opioid boluses, without needing to resort to controversial options like epidural infusions. It is also widely accepted that there are significant cost benefits to the fast tracking of cardiac patients and faster patient turnover, through an increased number of surgeries, can be achieved.

I therefore challenge you to view cardiac surgery as being a spectrum – FTCA on one side and high-dose opioid CCA on the other. We are unlikely in our current environment to achieve full fast track anaesthesia as has been done in true first world centres. Perhaps though, if we could shift our practice a little further down the road towards FTCA we can still reap some of the benefits it provides?

REFERENCES

1. Lowenstein E et al. Cardiovascular response to large doses of intravenous morphine in man. *NEJM* 1969; 281(25):1389–1392
2. Stanley T H; Webster L R. Anesthetic requirements and cardiovascular effects of fentanyl-oxygen and fentanyl-diazepam-oxygen anesthesia in man. *Anesth Analg* 1978;57:411–416
3. Myles P S et al. A systematic review of the safety and effectiveness of fast-track cardiac anesthesia. *Anesthesiology* 2003;99:982–987
4. Silbert B S; Myles P S. Is fast-track cardiac anesthesia now the global standard of care?. *Anesth Analg* 2009;108:689-691
5. Chen D C H. Fast-track cardiac surgery: economic implication in postoperative care. *J Cardiothorac Vasc Anesth* 1998;12:72-79
6. Djaiani G N et al. Ultra-fast-track anesthetic technique facilitates operating room extubation in patients undergoing off-pump coronary revascularisation surgery. *J Cardiothorac Vasc Anesth* 2001;15:152-157
7. Montes F et al. The Lack of Benefit of Tracheal Extubation in the Operating Room After Coronary Artery Bypass Surgery. *Anesth Analg* 2000;91:776–80
8. Peragallo R A, Cheng D C H. Con: Tracheal extubation should not occur routinely in the operating room after cardiac surgery. *J Cardiothorac Vasc Anesth* 2000;14:611-613
9. Constantinides V A. Fast-track failure after cardiac surgery: Development of a prediction model. *Crit Care Med* 2006;34:2875-2882
10. Svircevic V et al. Fast-Track Anesthesia and Cardiac Surgery: A Retrospective Cohort Study of 7989 Patients. *Anesth Analg* 2009;108:727- 733
11. Reis J et al. Early extubation does not increase complication rates after coronary artery bypass graft surgery with cardiopulmonary bypass. *Eur J Cardiothorac Surg* 2002;21:1026-1030
12. Bowler I et al. A Combination of Intrathecal Morphine and Remifentanyl Anesthesia for Fast-Track Cardiac Anesthesia and Surgery. *J Cardiothorac Vasc Anesthesia* 2002;16:709-714.
13. Howie M B et al. A Randomized Double-Blinded Multicenter Comparison of Remifentanyl Versus Fentanyl When Combined with Isoflurane/Propofol for Early Extubation in Coronary Artery Bypass Graft Surgery. *Anesth Analg* 2001;92:1084–1093
14. Cheng D C H et al. The Efficacy and Resource Utilization of Remifentanyl and Fentanyl in Fast-Track Coronary Artery Bypass Graft Surgery: A Prospective Randomized, Double-Blinded Controlled, Multi-Center Trial. *Anesth Analg* 2001;92:1094–1102

15. Molhoff t et al. Comparative efficacy and safety of remifentanil and fentanyl in 'fast track' coronary artery bypass graft surgery: a randomised, double blind study. *BJA* 2001; 87: 718 – 726
16. Hadjinikolaou L et al. The effect of a 'fast-track' unit on the performance of a cardiothoracic department. *Ann R Coll Surg Engl* 2000;82:53-58
17. Silbert B S et al. Early Extubation Following Coronary Artery Bypass Surgery. *Chest* 1998;113:1481-1488.
18. Chaney M A et al. Intrathecal morphine for coronary artery bypass grafting and early extubation. *Anesth Analg* 1997;84:241-248
19. Cheng D C H et al. Early tracheal extubation after coronary artery bypass graft surgery reduces costs and improves resource use. *Anesthesiology* 1996;85:1300-1310
20. Cheng D C H et al. Morbidity outcome in early versus conventional tracheal extubation after coronary artery bypass grafting: a prospective randomised control trial. *J Thorac Cardiovasc surg* 1996;112:755-764
21. Slogoff S, Keats A S. Randomised trial of primary anesthetic agents on outcome of coronary artery bypass operation. *Anesthesiology* 1989;70:179-188
22. Latham P et al. Fast-Track Cardiac Anesthesia: A Comparison of Remifentanil Plus Intrathecal Morphine With Sufentanil in a Desflurane-Based Anesth. *J Cardiothor Vasc Anesth* 2000;14:645-651.
23. Hawkes C A. Cochrane Review - Early extubation for adult cardiac surgical patients. 2003
24. van Mastrigt G A P G et al. Does fast-track treatment lead to a decrease of intensive care unit and hospital length of stay in coronary artery bypass patients? A meta-regression of randomized clinical trials. *Crit Care Med* 2006;34:1624-1634
25. Reyes A et al. Early vs. Conventional Extubation After Cardiac Surgery With Cardiopulmonary Bypass. *Chest* 1997;112:193-201
26. Nashef S A M et al. European system for cardiac operative risk evaluation (EuroSCORE). *Eur J Cardiothorac Surg* 1999;16: 9-13
27. Kogan A et al. Readmission to the Intensive Care Unit After "Fast-Track" Cardiac Surgery: Risk Factors and Outcomes. *Ann Thorac Surg* 2003;76:503-507
28. Bernstein A D, Parsonnet V. Bedside Estimation of Risk as an Aid for Decision- Making in Cardiac Surgery. *Ann Thorac Surg* 2000;69:823–8
29. Ender J et al. Cardiac Surgery Fast-track Treatment in a Postanesthetic Care Unit. *Anesthesiology* 2008;109:61–66
30. Myles P S et al. Hemodynamic Effects, Myocardial Ischemia, and Timing of Tracheal Extubation with Propofol-Based Anesthesia for Cardiac Surgery. *Anesth Analg* 1997;84:12-9
31. Flynn M et al. Fast-tracking revisited: routine cardiac surgical patients need minimal intensive care. *Eur J Cardiothorac Surg* 2004;25:116-122
32. Engoren M et al. A Comparison of Fentanyl, Sufentanil, and Remifentanil for Fast-Track Cardiac Anesthesia. *Anesth Analg* 2001;93:859 –64
33. Lison S et al. Fast-Track Cardiac Anesthesia: Efficacy and Safety of Remifentanil Versus Sufentanil. *J Cardiothorac Vasc Anesth* 2007;21:35-40
34. Dasta J F et al. Addition of dexmedetomidine to standard sedation regimens after cardiac surgery: an outcomes analysis. *Pharmacotherapy* 2006;26(6):798–805
35. Aantaa R, Jalonen J. Perioperative use of alpha 2 adrenoceptor agonists and the cardiac patient. *Eur J Anaesthesiol* 2006;23(5):361–372
36. Royse C et al. Prospective Randomized Trial of High Thoracic Epidural Analgesia for Coronary Artery Bypass Surgery. *Ann Thorac Surg* 2003;75:93–100
37. Westaby s et al. Does modern cardiac surgery require conventional intensive care? *Eur J Cardio-thorac Surg* 1993;7:313-318
38. Scott N B et al. A Prospective Randomized Study of the Potential Benefits of Thoracic Epidural Anesthesia and Analgesia in Patients Undergoing Coronary Artery Bypass Grafting. *Anesth Analg* 2001;93:528–35.
39. Chong J L et al. The effect of a cardiac surgical recovery area on the timing of extubation. *J Cardiothorac Vasc Anesth* 1993: 7: 137 – 141
40. Pande R U et al. Review Fast-Tracking Cardiac Surgery. *The Heart Surgery Forum* 2003 6 (4), 2003.
41. Chaney M A. Intrathecal and Epidural Anesthesia and Analgesia for Cardiac Surgery. *Anesth Analg* 2006;102:45–64
42. Poyhia R. Editorial: Cardiac surgery: with or without epidurals? *Acta Anaesthesiol Scand* 2006;50:777–779
43. Liu S S et al. Effects of perioperative central neuraxial analgesia on outcome after coronary artery bypass surgery: a meta-analysis. *Anaesthesiology* 2004;101:153–161
44. Ho A et al
45. Quasha A L et al. Postoperative respiratory care: a controlled trial of early and late extubation following coronary-artery bypass grafting. *Anesthesiology* 1980; 52:135-141
46. Foster G H et al. Early extubation after coronary artery bypass: brief report. *Crit Care Med* 1984;12:994–996
47. Cheng D C H et al. Randomized Assessment of Resource Use in Fast-track Cardiac Surgery 1-Year after Hospital Discharge. *Anesthesiology* 2003;98:651–7

NOTES